A New Medicine

- The endocannabinoid system is a therapeutic target yet to be properly explored for pain management
- Cannabinoids are a new medicine to clinicians
  - New role, effects, benefits, side-effects
- A new method of administration

But…
- Many of our patients are already using street Cannabis for symptom control using similar materials but different delivery systems.
Clinical Use of Cannabinoids

Focusing on Medicinal Products in use.

• Selecting Patients
• What to Tell Patients about Cannabinoids
• Prescribing Cannabinoids
• Further Management
• What If …..

Selecting Patients

Symptoms and Co-Morbidity
Other Potential Targets? (Licenced - L)

**Pain Problems**
- Neuropathic (L)
  - Central (L)
  - Peripheral (L)
- Cancer Pain (L)
- Nociceptive
- Idiopathic
  - Migraine
  - Perineal
  - Facial pain
  - Fibromyalgia

- Complex pain problems
  - HIV Neuropathy
  - “Failed Back”
  - Rheumatoid Arthritis

**Other Areas**
- Anti-emetic, CINV (L)
- Epilepsy
- Bladder dysfunction
- Anti-tumour
- Neuroprotection
- Appetite
- + others

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Medicinal Cannabinoids Licensed for Clinical Use

- Nabilone (Cesamet): synthetic THC analogue
  - CINV nausea and vomiting
- Dronabinol (Marinol): synthetic THC 2.5/5/10mg capsules
  - Appetite stimulation in AIDS
  - CINV nausea and vomiting
- Nabiximols (Sativex): plant extracted THC/CBD mixture
  - MS related spasticity/spasms
  - Cancer Pain
  - Neuropathic Pain
- Bedrocan (plant) and Namisol (plant THC tablet)
Origins of Pain in MS

- Neural damage to Brain
- Neural damage to Spinal Cord
- Visceral muscle spasm
- Mechanical Weakness, immobility
- Psycho-social factors
- Unrelated to MS
- Somatic muscle spasm, spasticity

Which Patients? : Complex not Simple

- **“End-of-the-Road”**
  - Add on therapy when all others are ineffective, insufficient or not tolerated (eg. Baclofen, Tizanidine, Gabapentin, Opiates)
  - Will try anything for relief

- **A New Treatment**
  - Pressure to prescribe
Which Patients? : General Factors

- **Age**
  - >18
  - Elderly
- **Frailty**
- **Weight/build**
- **Previous cannabis use**
  - What is acceptable?
    - Occasional recreational use when young
    - Smoking a cannabis cigarette at night to relieve symptoms
    - **Smoking cannabis 6x/day**
    - Regular recreational use
    - Dependency history

Which Patients? : Co-Morbidity

- **Cardiovascular Disease**
  - IHD
  - Hypertension
  - Dysrhythmias
  - Postural hypotension
  - Mixture of Medications
- **Respiratory Disease**
  - COPD – late stage

- **No known significant drug interactions**
Which Patients ? : Co-Morbidity

- Liver, Kidney
  - Tissue solubility, self administration
- CNS
  - Epilepsy
  - Psychosis, Endogenous Depression, Personality disorders
  - Cognitive problems (MS, Dementia etc)
  - Addiction/Abuse/Alcohol problems
  - Note: MS is associated with Suicide, Euthanasia and shorter life span
- Pregnancy

Preparing the Patient
Informing the Patients about Cannabinoids

- Endogenous Cannabinoids
  - Receptors and ligands and their role
- Medicinal Cannabinoid
  - Which one
- How is it given?
- Why am I prescribing it for you?
- Will I get ‘High’
- Will I become addicted

What to Tell Patients about Cannabinoids Side-Effects

- Common Side Effects
  - Drowsy, Dizzy, Light-Headed
    - Likely to have used other psychoactive drugs and had S/E
  - Importance of Titration
  - Too much cannabinoid
    - Go and lie down
    - Passes off in 2-3 hours
Unrelieved Symptoms $\rightarrow$ Side-Effects

*Immobile from MS*

*Immobile from Treatment*

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**What to Tell Patients about Cannabinoids**

**Side-Effects**

- **Less Common Side Effects**
  - Panic, anxiety
  - Euphoria
- **Other Side Effects**
  - Psychosis
  - Addiction
  - Cognitive Impairment, Memory loss
  - Increased appetite (Munchies)
  - Excessive Hypotonia
What to Tell Patients about Cannabinoids

Driving

- A common question
- Each Nation will have a different approach to this.
- Road Research Laboratory findings

- Other drugs
- Distraction by pain, spasms
- What happens when an accident occurs? Insurance
- Operating machinery etc.

Influence of Cannabis on Driving 1

1 “joint” equivalent to get “high”; tested in a driving simulator:

- Tracking tasks are affected
- Reaction times increased slightly

- Aware of impairment, therefore drive more slowly – unlike alcohol

Cannabis and Accidents

- **Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis (Recreational)**
  - Acute cannabis consumption nearly doubles the risk of a collision resulting in serious injury or death; this increase was most evident for studies of high quality, case-control studies, and studies of fatal collisions
  - The influence of cannabis use on the risk of minor collisions remains unclear
    - BMJ Editorial 2012;344: 3/3/12

- Any impairment is probably well within the range of (or lower than) what is currently produced by pharmaceutical agents which are commonly used for similar conditions. (Opiates, Benzodiazepines, Tricyclic Antidepressants, Baclofen, etc)

  Hadorn. *The Medicinal Uses of Cannabis and Cannabinoids*

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Prescribing Cannabinoids

Titration
Prescribing: Dronabinol

• 1 to 3 hours before chemotherapy →
  – and then every 2 to 4 hours after chemotherapy,
  – → 4 to 6 doses a day

• To increase appetite, 1-2 times a day – bd or nocte

Prescribing: Nabilone

• The usual dosage of Cesamet is 1 mg or 2 mg twice a day
• Nabilone should be given 1 to 3 hours before chemotherapy, and a dose given the night before
• Nabilone may be given for the entire course of each chemotherapy cycle and, if needed, for 48 hours after the last dose of each cycle.
• Capsule splitting
Prescribing: Sativex Oro-mucosal Spray

- **Titrating**
  - Factors for starting point
  - 1 spray/day increase
  - 4 hourly intervals

- **Customising to the pattern of pain/problem**
  - Day
  - Night
  - Break through Pain

- **Maximum Dose**
  - Up to 12 sprays/day Little benefit from increasing further

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**Using Sativex**

- **Using Sativex**
  - Sublingual
  - Buccal

- Keep the spray in the mouth for 5 minutes
  - Oral
Using Sativex

• Mouth Problems
  – Unpleasant taste
  – Retching – milk option
  – Dry Mouth
  – Sting, ulcer
    • Stomatitis
  – High volume of spray
  – When to eat or drink
    • Keep the spray in the mouth for 5 minutes

Prescribing: Bedrocan

• Smoking of cannabis is not recommended.
• Instead of smoking a vaporizer can be used to inhale cannabis vapor.
• Also ingestion of cannabis as a herbal tea is recommended.
Further Management

Evaluating Effect

• Every Patient is Different in Symptoms and Response
  ➔ Decide which parameters to use:
    – **Consider NRS (Numerical Rating Score 0-10) etc.**

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<th>Spasticity, Spasms</th>
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<td>Work, pastimes etc</td>
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<td>Changes in other drug use</td>
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<td>Bowels, sex</td>
<td>Improvements for Carers</td>
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<td>Other Neuro symptoms</td>
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</table>
Evaluating Side-Effects

- Sedation,
- Dizzy, Light headed
- Anxiety, Panic
- Hypotonia
- Euphoria etc.
- Check Oral Mucosa (Sativex)

Managing the Other Analgesics etc.

- Baclofen, Tizanidine
- Tricyclic Antidepressants
- Gabapentin/Pregabalin/Carbamazepine etc.
- Opioids

- Reducing / Increasing
What If…?

- Patient has an injury causing pain
- Patient needs to come into hospital for surgery
- Patient is admitted for a medical emergency
- Patient wants to go abroad on holiday
- Patient wants a break from the medicine
Misuse

• Diversion
  – Stolen
    • Don’t tell the neighbours
  – Deliberate by the patient to sell on
    • Depends on the current street price
    • Ensure patients return empty bottles?
    • Increasing use of drug = diversion
      until proved otherwise
  – Deliberate by patient to provide a
    personal, legitimate recreational
    drug source
    • The “High” is better with smoking

The Doctors

• Ensure that Doctors:
  – Learn about the medicine
  – Choose appropriate patients
  – Instruct the patient correctly
  – Ensure appropriate titration and
    later customisation
  – Assess the benefits of other
    medicines
  – Monitor the long term effects/
    benefits
Other Problems.....

• Cost of the Medicines

• Cost of other MS medicines
• Attitudes to Cannabinoids